DOCUMENT NUMBER: PREV199395073538
TITLE: The Drosophila **hedgehog** gene is expressed specifically in posterior compartment cells and is a target of engrailed regulation.
AUTHOR(S): Tabata, Tetsuya; Eaton, Suzanne; Kornberg, Thomas B.
CORPORATE SOURCE: Dep. Biochem. Biophysics, Univ. Calif., San Francisco, CA 94143 USA
SOURCE: Genes & Development, (1992) Vol. 6, No. 12B, pp. 2635-2645.
ISSN: 0890-9369.
DOCUMENT TYPE: Article
LANGUAGE: English
AB cDNAs were isolated that represent transcripts of the Drosophila segment polarity gene, **hedgehog** (hh). Sequence analysis reveals a motif characteristic of a transmembrane domain, suggesting that the hh protein is membrane-associated. hh expression in epidermal cells is confined to the posterior compartments and coincides precisely with that of engrailed (en). Despite the similar patterns of expression in the cellular blastoderm, hh expression is independent of en, but hh expression becomes sensitive to and dependent on en during the extended germ band stage. The ectopic expression of hh that is normally induced in patched (**ptc**) mutant embryos does not appear in **ptc** en double mutants. We discuss these findings in terms of the relationship between en and hh, and the role of the hh function.

L29 ANSWER 25 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 22
ACCESSION NUMBER: 1992:49477 BIOSIS
DOCUMENT NUMBER: BA93:29452
TITLE: INTERACTIONS BETWEEN SEGMENT POLARITY GENES AND THE GENERATION OF THE SEGMENTAL PATTERN IN DROSOPHILA.
AUTHOR(S): HIDALGO A
CORPORATE SOURCE: CENTRO DE BIOLOGIA MOLECULAR-CSIC, UNIVERSIDAD AUTONOMA DE MADRID, CANTOBLANCO, MADRID 28049, SPAIN.
SOURCE: MECH DEV, (1991) 35 (2), 77-88.
CODEN: MEDVE6. ISSN: 0925-4773.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Although mutations in the segment polarity genes wingless, engrailed, **hedgehog**, gooseberry and cubitus-interruptusD all affect the region of naked cuticle within each segment of the Drosophila larva, subtle phenotypic differences suggest that these genes play different roles in segmental patterning. In this paper, the regulative interactions between these genes are analysed. They have revealed that the products of most of these genes accomplish more than one function during embryogenesis. Whereas early on a positive feed-back loop involving wg, en and hh maintains the expression of wg and en in the extremes of each parasegment, later on wg and en become independent from each other. en appears to regulate the expression of hh and **ptc**, while wg depends on gsb and ciD.

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 NEWS  4  Feb 16   TOXLINE no longer being updated
 NEWS  5  Apr 23   Search Derwent WPINDEX by chemical structure
 NEWS  6  Apr 23   PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
 NEWS  7  May 07   DGENE Reload
 NEWS  8  Jun 20   Published patent applications (A1) are now in USPATFULL
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L1 13 "HEDGEHOG POLYPEPTIDE?"

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L2 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:417124 CAPLUS
DOCUMENT NUMBER: 135:45164
TITLE: Methods and compositions for regulating lymphocyte activity
INVENTOR(S): Crompton, Tessa
PATENT ASSIGNEE(S): Curis, Inc., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040438	A2	20010607	WO 2000-US32590	20001130

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-168112 P 19991130
OTHER SOURCE(S): MARPAT 135:45164
AB The present application is directed to the discovery that hedgehog gene products, and signal transduction pathways involving hedgehog, are involved in maturation of T lymphocytes. Certain aspects of the invention are directed to prepns. of **hedgehog polypeptides**, agonists, antagonists, or other mols. which regulate patched or smoothened signalling, and their uses as immunomodulatory agents.

L2 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:257989 CAPLUS
DOCUMENT NUMBER: 134:275773
TITLE: Method of using **hedgehog polypeptides** to regulate neuronal cell growth
INVENTOR(S): Beachy, Philip A.; Moon, Randall T.; Porter, Jeffrey A.
PATENT ASSIGNEE(S): The Johns Hopkins University School of Medicine, USA; University of Washington
SOURCE: U.S., 78 pp., Cont.-in-part of U.S. Ser. No. 567,357. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6214794	B1	20010410	US 1996-729743	19961007
US 6132728	A	20001017	US 1995-567357	19951204
WO 9830576	A1	19980716	WO 1997-US15753	19971007
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9748006	A1	19980803	AU 1997-48006	19971007
AU 728541	B2	20010111		
EP 966478	A1	19991229	EP 1997-910705	19971007
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6057091	A	20000502	US 1997-946329	19971007

PRIORITY APPLN. INFO.:
US 1994-349498 A2 19941202
US 1995-567357 A2 19951204
US 1996-729743 A2 19961007
US 1997-61323 P 19971002
WO 1997-US15753 W 19971007

AB The present invention provides two novel polypeptides, referred to as the N and C fragments of hedgehog, or N-terminal and C-terminal fragments, resp., which are derived after specific cleavage at a Gly.dwnarw.CysPhe site recognized by the autoproteolytic domain in the native protein. Methods of identifying compns. which affect hedgehog activity based on inhibition of cholesterol modification of hedgehog protein are described. Also provided are methods of use of the N and C fragments.

REFERENCE COUNT: 17
REFERENCE(S):
(1) Clarke; FESEB J 1989, V3, P2480 CAPLUS
(2) Echelard; Cell 1993, V75, P1417 CAPLUS
(5) Holland; US 5143830 1992 CAPLUS
(6) Hynes; Neuron 1995, V15, P35 CAPLUS
(7) Ingham; US 5789543 1998 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 10 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1
ACCESSION NUMBER: 2000:489239 BIOSIS
DOCUMENT NUMBER: PREV200000489360
TITLE: Method of identifying compounds affecting hedgehog cholesterol transfer.
AUTHOR(S): Beachy, Philip A. (1); Porter, Jeffrey A.
CORPORATE SOURCE: (1) Baltimore, MD USA
ASSIGNEE: The Johns Hopkins University School of Medicine, Alexandria, VA, USA
PATENT INFORMATION: US 6057091 May 02, 2000

SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (May 2, 2000) Vol. 1234, No. 1, pp. No pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

AB The present invention provides two novel polypeptides, referred to as the "N" and "C" fragments of hedgehog, or N-terminal and C-terminal fragments, respectively, which are derived after specific cleavage at a Gdwnarw CF site recognized by the autoproteolytic domain in the native protein. Also included are sterol-modified **hedgehog polypeptides** and functional fragments thereof. Methods of identifying compositions which affect hedgehog activity based on inhibition of cholesterol modification of hedgehog protein are described.

L2 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:861709 CAPLUS
DOCUMENT NUMBER: 134:32958
TITLE: Polymer conjugates of hedgehog proteins and uses
INVENTOR(S): Pepinsky, R. Blake; Taylor, Frederick; Garber, Ellen
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: PCT Int. Appl., 157 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073337	A1	20001207	WO 2000-US14741	20000526

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-137011 P 19990601
US 1999-149016 P 19990813

AB A **hedgehog polypeptide** comprising hedgehog coupled to a polymer contg. a polyalkylene glycol moiety wherein the hedgehog and the polyalkylene glycol moiety are arranged such that the hedgehog has an enhanced bioavailability relative to another hedgehog lacking the polymer and exhibits no decrease in activity as compared to non-conjugated hedgehog. The conjugates of the invention are usefully employed in therapeutic as well as non-therapeutic, e.g., diagnostic, applications.

REFERENCE COUNT: 7
REFERENCE(S):
(1) Beachy, P; WO 9830576 A 1998 CAPLUS
(2) Ontogeny Inc; WO 9910004 A 1999 CAPLUS
(3) Ontogeny Inc; WO 9920298 A 1999 CAPLUS
(4) Porter; SCIENCE 1996, V274, P255 CAPLUS
(5) Roche Diagnostics Gmbh; EP 0953576 A 1999 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:421167 CAPLUS
DOCUMENT NUMBER: 133:68974
TITLE: Methods and compositions using **hedgehog polypeptides** for treating disorders involving excitotoxicity
INVENTOR(S): Galdes, Alphonse; Mahanthappa, Nagesh

PATENT ASSIGNEE(S): Biogen, Inc., USA; Ontogeny, Inc.
SOURCE: PCT Int. Appl., 174 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035948	A1	20000622	WO 1999-US28721	19991203
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 9928343	A2	19990610	WO 1998-US25676	19981203
WO 9928343	A3	19990812		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

WO 1998-US25676	W	19981203
US 1999-238243	A	19990127
US 1999-325602	A	19990603
US 1997-67423	P	19971203
US 1998-78935	P	19980320
US 1998-89685	P	19980617
US 1998-99800	P	19980910

AB It is shown here that **hedgehog polypeptides** possess activities beyond phenotype specification. Using cultures derived from the embryonic day 14.5 (E14.5) rat ventral mesencephalon, we show that hedgehog is also trophic for dopaminergic neurons and other neurons which are sensitive to excitotoxicity.

REFERENCE COUNT: 8
REFERENCE(S):
(1) Beachy, P; WO 9830576 A 1998 CAPLUS
(2) Porter; SCIENCE 1996, V274, P255 CAPLUS
(3) Roche Diagnostics Gmbh; EP 0953575 A 1999 CAPLUS
(4) Roche Diagnostics Gmbh; EP 0953576 A 1999 CAPLUS
(5) Strauch, K; WO 9928343 A 1999 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:335263 CAPLUS
DOCUMENT NUMBER: 133:813
TITLE: Methods and compositions for treating or preventing peripheral neuropathies
INVENTOR(S): Galdes, Alphonse; Mahanthappa, Nagesh
PATENT ASSIGNEE(S): Biogen, Inc., USA; Ontogeny, Inc.
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000027422 A2 20000518 WO 1999-US26334 19991108
WO 2000027422 A3 20001109
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 1998-187387 A 19981106
OTHER SOURCE(S): MARPAT 133:813
AB The present application is directed to the discovery that hedgehog gene products are able to protect peripheral nerve cells under conditions which otherwise result in peripheral neuropathy. Certain aspects of the invention are directed to prepns. of **hedgehog polypeptides**, or other mols. which regulate patched or smoothened signalling, and their uses as protective agents against both acquired and hereditary neuropathies. As used herein, "peripheral neuropathy" refers to a disorder affecting a segment of the peripheral nervous system. For instance, the method of the present invention can be used as part of a treatment program in the management of neuropathies assocd. with systemic disease, e.g., viral infections, diabetes, inflammation; as well as genetically acquired (hereditary) neuropathies, e.g., Charcot-Marie-Tooth disease; and neuropathies caused by a toxic agent, e.g., a chemotherapeutic agent such as vincristine.

L2 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:640959 CAPLUS
DOCUMENT NUMBER: 131:283610
TITLE: Method for identifying inhibitors of proteoglycan-dependent signal transduction of growth factors and cytokines
INVENTOR(S): Bellaiche, Yohanns; The, Siu Inge; Perrimon, Norbert
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9950385	A2	19991007	WO 1999-US6892	19990330

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 1998-79928 P 19980330
AB The title method comprises (1) providing a reaction mixt. contg. a glycosyltransferase which is essential to synthesis of a proteoglycan and which selectively regulates the signal transduction activity of the growth factor or cytokine, a substrate for the glycosyltransferase, and a test agent under conditions in which the glycosyltransferase converts the substrate to a detectable product in the absence of the test agent; and (2) detecting the conversion of substrate to product. A decrease in rate of conversion of substrate to product in the presence of the test compd.,

relative to its absence, indicates that the test compd. is an inhibitor of the glycosyltransferase. The present invention concerns the discovery of a new family of hedgehog interacting proteins, referred to as Ext's, which are demonstrated to bind to **hedgehog polypeptides** with high affinity. The Ext proteins are required for and as such regulate hedgehog diffusion. The ext genes encode a family of glycosyltransferases which synthesize GAG chains attached to the protein core of proteoglycans. In Drosophila wing imaginal disks, Hh was unable to diffuse from the posterior to the anterior compartment in the absence of activity of the ext gene ttv. In an addnl. expt., characterization of the Drosophila gene sulfateless, which encodes a homolog of a vertebrate heparan sulfate (HS) N-deacetylase/N-sulfotransferase, revealed that HS proteoglycans are necessary for Wg/Wnt signaling. The GPI-linked glypican, Dally, was identified as the proteoglycan involved in Wg signaling. The gene dally is coexpressed with the Wg receptor frizzled 2, so Dally may serve as coreceptor for the Wnt receptor.

L2 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:490651 CAPLUS
DOCUMENT NUMBER: 129:119314
TITLE: Autoproteolytic and sterol-modified hedgehog-derived polypeptides
INVENTOR(S): Beachy, Philip A.; Porter, Jeffrey A.
PATENT ASSIGNEE(S): The Johns Hopkins University School of Medicine, USA; Beachy, Philip A.; Porter, Jeffrey A.
SOURCE: PCT Int. Appl., 210 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9830576	A1	19980716	WO 1997-US15753	19971007
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6214794	B1	20010410	US 1996-729743	19961007
AU 9748006	A1	19980803	AU 1997-48006	19971007
AU 728541	B2	20010111		
EP 966478	A1	19991229	EP 1997-910705	19971007
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:

US 1996-729743	A2	19961007
US 1997-61323	P	19971002
US 1994-349498	A2	19941202
US 1995-567357	A2	19951204
WO 1997-US15753	W	19971007

AB The present invention provides 2 novel polypeptides, referred to as the "N" and "C" fragments of hedgehog, or N-terminal and C-terminal fragments, resp., which are derived after specific cleavage at a G.dwnarw.CF site recognized by the autoproteolytic domain in the native protein. Hedgehog proteins undergo auto-proteolytic cleavage which results in 2 sep. proteins having distinct functional and structural characteristics. The C

fragment functions as a cholesterol transferase during autoproteolysis thus allowing cholesterol modification of the N fragment. Also included are sterol-modified **hedgehog polypeptides** and functional fragments thereof. Hedgehog precursor protein and the autoproteolytic products of hedgehog precursor protein are expressed in the floorplate of the ventral midline of the neural tube and notochord, and may be used for the induction of proliferation or differentiation of neuronal cells assocd. with or in close proximity to these tissues. The tissue localization and developmental roles of hedgehog proteins are described in Drosophila melanogaster, zebrafish (Danio rerio), Xenopus laevis, chicken, mouse, and human. Methods of identifying compns. which affect hedgehog activity based on inhibition of cholesterol modification of hedgehog protein are described. In addn., x-ray diffraction of Drosophila hedgehog protein provide information for 3-dimensional conformational anal. and the modeling design of modulator compds.

L2 ANSWER 9 OF 10 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:21474 BIOSIS
DOCUMENT NUMBER: PREV199800021474
TITLE: Cancer genes and cell signalling.
AUTHOR(S): Bishop, J. Michael (1)
CORPORATE SOURCE: (1) G. W. Hooper Res. Foundation, Univ. Calif., San Francisco, CA 94143 USA
SOURCE: Molecular Biology of the Cell, (Nov., 1997) Vol. 8, No. SUPPL., pp. 353A.
Meeting Info.: 37th Annual Meeting of the American Society for Cell Biology Washington, D.C., USA December 13-17, 1997
American Society for Cell Biology
. ISSN: 1059-1524.
DOCUMENT TYPE: Conference
LANGUAGE: English

L2 ANSWER 10 OF 10 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2
ACCESSION NUMBER: 1995:457856 BIOSIS
DOCUMENT NUMBER: PREV199598472156
TITLE: Patterning of the neural ectoderm of Xenopus laevis by the amino-terminal product of hedgehog autoproteolytic cleavage.
AUTHOR(S): Lai, Cheng-Jung; Ekker, Stephen C.; Beachy, Philip A.; Moon, Randall T. (1)
CORPORATE SOURCE: (1) Dep. Pharmacol., Univ. Washington Sch. Med., Seattle, WA 98195 USA
SOURCE: Development (Cambridge), (1995) Vol. 121, No. 8, pp. 2349-2360.
ISSN: 0950-1991.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The patterns of embryonic expression and the activities of Xenopus members of the hedgehog gene family are suggestive of roles in neural induction and patterning. We report that these **hedgehog polypeptides** undergo autoproteolytic cleavage. Injection into embryos of mRNAs encoding Xenopus banded-hedgehog (X-bhh) or the amino-terminal domain (N) demonstrates that the direct inductive activities of X-bhh are encoded by N. In addition, both N and Xbhh pattern neural tissue by elevating expression of anterior neural genes. Unexpectedly, an internal deletion of X-bhh (DELTA-N-C) was found to block the activity of X-bhh and N in explants and to reduce dorsoanterior structures in embryos. As elevated hedgehog activity increases the expression of anterior neural genes, and as DELTA-N-C reduces dorsoanterior structures, these complementary data support a role for hedgehog in neural induction and anteroposterior patterning.

```
=> s polypeptide?

L3      276309 POLYPEPTIDE?

=> s l3 and "hedgehog?"

L4          73 L3 AND "HEDGEHOG?"

=> s "hedgehog?"

L5        6915 "HEDGEHOG?"

=> s l5 and l3

L6          73 L5 AND L3

=> s "ptc therapeutic?"

L7           8 "PTC THERAPEUTIC?"

=> dup rem

ENTER L# LIST OR (END):l7

DUPLICATE IS NOT AVAILABLE IN 'CAOLD'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L7
L8           8 DUP REM L7 (0 DUPLICATES REMOVED)

=> d l8 1-8 ibib abs


L8   ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2001:449178  CAPLUS
DOCUMENT NUMBER:          135:51158
TITLE:                    Therapeutic antimicrobial compositions
INVENTOR(S):              Jampani, Hanuman B.; Newman, Jerry L.; Ellis, Timothy
PATENT ASSIGNEE(S):       Ethicon, Inc., USA
SOURCE:                   U.S., 14 pp., Cont.-in-part of U.S. 6,022,551.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   3
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
     US 6248343         B1   20010619       US 1999-460031    19991213
     US 6022551         A    20000208       US 1998-9596      19980120
     AU 9912158         A1   19990812       AU 1999-12158     19990119
     CN 1232665         A    19991027       CN 1999-100879    19990120
     JP 11322560        A2   19991124       JP 1999-48718     19990120
     BR 9900320         A    20000516       BR 1999-320       19990121
     WO 2001041573      A1   20010614       WO 2000-US33928   20001213
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                  US 1998-9596      A2 19980120
                                        US 1999-460031    A  19991213
```

AB Antimicrobial compns. comprise :(a) and alc. and/or triclosan; (b) phenoxyethanol, benzalkonium chloride or benzethonium chloride and cocophosphatidyldimonium chloride; ans (c) a plant material or plant ext. The compns. are applied to the skin and are effective for the treatment of acne, inflammations, pseudofolliculitis, etc. The plants used are Curcuma longa, Crocus sativus, Alkanna tinctoria and Hydrastis canadensis.
REFERENCE COUNT: 96
REFERENCE(S): (1) Anon; EP 0099209 1984 CAPLUS
(2) Anon; EP 0223681 B1 1987 CAPLUS
(3) Anon; EP 0231080 1987 CAPLUS
(4) Anon; AU 600269 1987 CAPLUS
(5) Anon; EP 0252278 B1 1988 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 8 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:236356 BIOSIS
DOCUMENT NUMBER: PREV200100236356
TITLE: A simple grading scale to assess ERCP technical difficulty:
An attempt to produce qualitative outcome data.
AUTHOR(S): Ragunath, K. (1); Thomas, L. A. (1); Cheung, W. Y.; Richards, D. G.; Duane, P. D. (1)
CORPORATE SOURCE: (1) Dept of Gastroenterology, Morriston Hospital, Swansea UK
SOURCE: Gut, (March, 2001) Vol. 48, No. Supplement 1, pp. A96-A97. print.
Meeting Info.: Annual Meeting of the British Society of Gastroenterology Glasgow, Scotland March 18, 2001-March 21,
2002 British Society of Gastroenterology
. ISSN: 0017-5749.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L8 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:539098 CAPLUS
TITLE: Private company profiles: **PTC therapeutics**
AUTHOR(S): Fletcher, Liz
SOURCE: Nat. Biotechnol. (2001), 19(Suppl.), BE14
CODEN: NABIF9; ISSN: 1087-0156
PUBLISHER: Nature America Inc.
DOCUMENT TYPE: Journal; Miscellaneous
LANGUAGE: English
AB Unavailable

L8 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:880985 CAPLUS
DOCUMENT NUMBER: 134:37058
TITLE: Therapeutic use of an inhibitor of a hedgehog or a hedgehog-related signaling pathway
INVENTOR(S): Lamb, Jonathan Robert; Hoyne, Gerard Francis; Dallman, Margaret Jane
PATENT ASSIGNEE(S): Lorantis Limited, UK
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000074706	A1	20001214	WO 2000-GB2191	20000605	

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-13350 A 19990608
GB 1999-21953 A 19990916

AB Use of an inhibitor of a Hedgehog signaling pathway, or an inhibitor of a pathway which is a target of the Hedgehog signaling pathway in the prepn. of a medicament for treatment of epithelial cell hyperplasia, fibrosis of tissue, inflammation, cancer or an immune disorder. Also a transgenic animal or cell line capable of expressing a component or an inhibitor of a hedgehog signaling pathway or a target pathway of the hedgehog signaling pathway.

REFERENCE COUNT: 8
REFERENCE(S):
(1) Deutsches Krebsforschungszentrum Stiftung Des Offentlichen Rechts; WO 9922000 A 1999 CAPLUS
(3) Fujita, E; BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS 1997, V238(2), P658 CAPLUS
(4) Johns Hopkins University School Of Medicine; WO 9952534 A 1999 CAPLUS
(5) Kabushiki Kaisha Hayashibara Seibutsu Kagaku Kenkyujo; EP 0874048 a 1998 CAPLUS
(6) Murone, M; CURRENT BIOLOGY 1999, V9(2), P76 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:190944 CAPLUS
DOCUMENT NUMBER: 132:231946
TITLE: Regulation of lung tissue by hedgehog-like polypeptides, and formulations and uses related thereto
INVENTOR(S): Pepicelli, Carmen; Lewis, Paula; McMahon, Andrew P.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015246	A2	20000323	WO 1999-US20500	19990910
WO 2000015246	A3	20000720		

W: AU, CA, JP, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AU 9962441	A1	20000403	AU 1999-62441	19990910
EP 1109569	A2	20010627	EP 1999-949603	19990910

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.: US 1998-99952 P 19980911
WO 1999-US20500 W 19990910

AB The present application relates to a method for modulating the growth state of a lung tissue, or a cell thereof, e.g., by ectopically contacting the tissue, in vitro or in vivo , with a hedgehog therapeutic, a

ptc therapeutic, or an FGF-10 therapeutic in an amt. effective to alter the rate (promote or inhibit) of proliferation of cells in the lung tissue, e.g., relative to the absence of administeration of the hedgehog therapeutic or **ptc therapeutic**. The subject method can be used, for example, to modulate the growth state of epithelial and/or mesenchymal cells of a lung tissue, such as may be useful as part of a regimen for prevention of a disease state, or in the treatment of an existing disease state or other damage to the lung tissue.

L8 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:282115 CAPLUS
DOCUMENT NUMBER: 130:320865
TITLE: Regulation of epithelial tissue by hedgehog-like polypeptides for stimulation of skin or hair formation
INVENTOR(S): Wang, Elizabeth A.
PATENT ASSIGNEE(S): Ontogeny, Inc., USA
SOURCE: PCT Int. Appl., 146 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920298	A1	19990429	WO 1998-US22227	19981020
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9911089	A1	19990510	AU 1999-11089	19981020
EP 1028741	A1	20000823	EP 1998-953814	19981020
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-955552 A 19971020
US 1998-151999 A 19980911
WO 1998-US22227 W 19981020
OTHER SOURCE(S): MARPAT 130:320865
AB The present application relates to a method for modulating the growth state of an epithelial cell by ectopically contacting the epithelial cell, in vitro or in vivo, with a hedgehog therapeutic or **ptc therapeutic** in an amt. effective to alter the rate (promote or inhibit) of proliferation of the epithelial cell, e.g., relative to the absence of administration of the hedgehog therapeutic or ptc (patched gene) therapeutic. The subject method can be used, for example, to modulate the growth state of an epithelial tissue, such as for inducing the formation of skin or other cutaneous tissue, or for inducing growth of hair.
REFERENCE COUNT: 20
REFERENCE(S):
(2) Anon; GROWTH STIMULATORS OF KERATINOCYTE AND EPIDERMAL FIBROBLASTS 1993, 10, CAPLUS
(3) Anon; HAIR GROWTH STIMULANTS CONTAINING PROTEIN KINASE-INHIBITING SULFONAMIDES 1991, 24, CAPLUS
(4) Anon; HAIR TONICS CONTAINING CYCLIC AMP DERIVATIVES 1989, 22, CAPLUS
(5) Chugai Pharmaceutical Co; JP 02273610 A 1990 CAPLUS

(6) Daiichi Seiyaku; JP 63088112 A 1988 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:172613 CAPLUS
DOCUMENT NUMBER: 130:205165
TITLE: Regulation of muscle tissue formation and/or maintenance with hedgehog proteins and **ptc therapeutics** and treatment or prevention of muscular disorders
INVENTOR(S): Bladgen, Chris S.; Currie, Peter D.; Ingham, Philip W.; Hughes, Simon M.
PATENT ASSIGNEE(S): Ontogeny, Inc., USA
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9910004	A2	19990304	WO 1998-US17922	19980828
WO 9910004	A3	19990527		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9891252	A1	19990316	AU 1998-91252	19980828
EP 1009424	A2	20000621	EP 1998-943462	19980828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-57394 P 19970829
WO 1998-US17922 W 19980828
OTHER SOURCE(S): MARPAT 130:205165
AB The present application relates to a method for modulating the formation and/or maintenance of muscle tissue by ectopically contacting muscle cells, esp. muscle stem/progenitor cells, in vitro or in vivo, with a hedgehog therapeutic or **ptc therapeutic** in an amt. effective to alter the growth state of the treated cells. The hedgehog therapeutic comprises a hedgehog protein modified with one or more lipophilic moieties, e.g., sterols, fatty acids, or arom. hydrocarbons. The **ptc therapeutics** mimic hedgehog-mediated patched signal transduction by binding to patched or altering localization, protein-protein binding and/or enzymic activity of intracellular proteins involved in patched signal transduction. Such therapeutics included antisense oligonucleotides and protein kinase A inhibitors. Expts. in zebrafish suggested that SHH may initiate slow myoblast formation but that continued exposure is not required to trigger terminal differentiation of slow muscle fibers.

L8 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:34842 CAPLUS
DOCUMENT NUMBER: 130:105320
TITLE: Neuroprotective hedgehog proteins and **ptc therapeutics** (agents mimicing effects of hedgehog proteins on patched signalling) for treatment of stroke
INVENTOR(S): Mahanthappa, Nagesh K.
PATENT ASSIGNEE(S): Ontogeny, Inc., USA

SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9900117	A2	19990107	WO 1998-US13387	19980626
WO 9900117	A3	19990401		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9881730	A1	19990119	AU 1998-81730	19980626

PRIORITY APPLN. INFO.: US 1997-883656 19970627
WO 1998-US13387 19980626
OTHER SOURCE(S): MARPAT 130:105320

AB One aspect of the present application relates to a method for limiting damage to neuronal cells from ischemic or epoxic conditions, e.g., such as
may be manifest by a redn. in brain infarct vol., by administering to an individual a hedgehog therapeutic or **ptc therapeutic** in an amt. effective for reducing cerebral infarct vol.

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(FILE 'HOME' ENTERED AT 15:38:29 ON 12 AUG 2001)

FILE 'BIOSIS, MEDLINE, CAPLUS, CAOLD' ENTERED AT 15:38:46 ON 12 AUG 2001
L1 13 S "HEDGEHOG POLYPEPTIDE?"
L2 10 DUP REM L1 (3 DUPLICATES REMOVED)
L3 276309 S POLYPEPTIDE?
L4 73 S L3 AND "HEDGEHOG?"
L5 6915 S "HEDGEHOG?"
L6 73 S L5 AND L3
L7 8 S "PTC THERAPEUTIC?"
L8 8 DUP REM L7 (0 DUPLICATES REMOVED)

=> s l5 and "ptc?"

L9 376 L5 AND "PTC?"

=> s l5 and "ptc therapeutic?"

L10 5 L5 AND "PTC THERAPEUTIC?"

=> dup rem

ENTER L# LIST OR (END):l9

DUPLICATE IS NOT AVAILABLE IN 'CAOLD'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L9
L11 177 DUP REM L9 (199 DUPLICATES REMOVED)

=> d l11 and "therapeutic?"

'AND' IS NOT A VALID FORMAT

'"THERAPEUTIC?"' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files. Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):s

'S' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files. Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):sl11

'SL11' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files. Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):d l11

'D' IS NOT A VALID FORMAT
'L43' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files. Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):ibib abs

L11 ANSWER 1 OF 177 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:417124 CAPLUS
DOCUMENT NUMBER: 135:45164
TITLE: Methods and compositions for regulating lymphocyte activity
INVENTOR(S): Crompton, Tessa
PATENT ASSIGNEE(S): Curis, Inc., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040438	A2	20010607	WO 2000-US32590	20001130

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-168112 P 19991130
OTHER SOURCE(S): MARPAT 135:45164
AB The present application is directed to the discovery that **hedgehog** gene products, and signal transduction pathways involving **hedgehog**, are involved in maturation of T lymphocytes. Certain aspects of the invention are directed to prepns. of **hedgehog** polypeptides, agonists, antagonists, or other mols. which regulate patched or smoothened signalling, and their uses as immunomodulatory agents.

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=> d his

     (FILE 'HOME' ENTERED AT 15:38:29 ON 12 AUG 2001)

     FILE 'BIOSIS, MEDLINE, CAPLUS, CAOLD' ENTERED AT 15:38:46 ON 12 AUG 2001
L1            13 S "HEDGEHOG POLYPEPTIDE?"
L2            10 DUP REM L1 (3 DUPLICATES REMOVED)
L3        276309 S POLYPEPTIDE?
L4            73 S L3 AND "HEDGEHOG?"
L5          6915 S "HEDGEHOG?"
L6            73 S L5 AND L3
L7             8 S "PTC THERAPEUTIC?"
L8             8 DUP REM L7 (0 DUPLICATES REMOVED)
L9           376 S L5 AND "PTC?"
L10            5 S L5 AND "PTC THERAPEUTIC?"
L11          177 DUP REM L9 (199 DUPLICATES REMOVED)

=> s l11 and "therapeutic?"

L12          10 L11 AND "THERAPEUTIC?"

=> d l12 1-10 ibib abs


L12  ANSWER 1 OF 10  BIOSIS  COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER:    2001:88175  BIOSIS
DOCUMENT NUMBER:     PREV20010008175
TITLE:               Cooperative effects of sonic hedgehog and NGF on
                     basal forebrain cholinergic neurons in vitro.
AUTHOR(S):           Reilly, J. O. (1); Mahanthappa, N. K.; Allendoerfer, K. L.
CORPORATE SOURCE:    (1) Ontogeny, Inc., Cambridge, MA USA
SOURCE:              Society for Neuroscience Abstracts, (2000) Vol. 26, No.
                     1-2, pp. Abstract No.-319.9. print.
                     Meeting Info.: 30th Annual Meeting of the Society of
                     Neuroscience New Orleans, LA, USA November 04-09, 2000
                     Society for Neuroscience
                     . ISSN: 0190-5295.
DOCUMENT TYPE:       Conference
LANGUAGE:            English
SUMMARY LANGUAGE:    English
AB   Sonic hedgehog (Shh) is a secreted protein that acts as an
     inducing molecule early in the development of the ventral neuraxis. Shh
     mediates the specification of several neural populations including spinal
     motor neurons, dopaminergic neurons, and cholinergic neurons during
     embryonic development. Since the Shh receptor patched-1 (Ptc-1)
     is also expressed by basal forebrain cholinergic neurons in early
     postnatal and adult life, we asked whether these neurons can respond to
     exogenously added Shh in vitro. We added Shh alone and in combination
with
     other growth factors to cultures derived from embryonic day 16 rat basal
     forebrain. We find that Shh treatment alone has no effect, but that Shh
     synergizes with nerve growth factor (NGF), increasing the number of
     choline acetyltransferase (ChAT) positive cells by four-fold over the
     untreated cultures and two-fold over NGF alone. Using 3H-thymidine
     incorporation combined with ChAT immunohistochemistry, we find that this
     synergistic effect does not appear to be the result of enhanced
     proliferation of early cholinergic precursors. Given the previous reports
     of the role of Shh in differentiation of neurons, it is hypothesized that
     the effects observed are due to increased differentiation or survival of
     cholinergic neurons in these cultures in response to Shh and NGF. These
     experiments imply a role for Shh in mature cells and suggests a
     therapeutic value for Shh in neurodegenerative disease.

L12  ANSWER 2 OF 10  CAPLUS  COPYRIGHT 2001 ACS
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ACCESSION NUMBER: 2000:880985 CAPLUS
DOCUMENT NUMBER: 134:37058
TITLE: **Therapeutic** use of an inhibitor of a **hedgehog** or a **hedgehog**-related signaling pathway
INVENTOR(S): Lamb, Jonathan Robert; Hoyne, Gerard Francis; Dallman, Margaret Jane
PATENT ASSIGNEE(S): Lorantis Limited, UK
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000074706	A1	20001214	WO 2000-GB2191	20000605

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-13350 A 19990608
GB 1999-21953 A 19990916

AB Use of an inhibitor of a **Hedgehog** signaling pathway, or an inhibitor of a pathway which is a target of the **Hedgehog** signaling pathway in the prepn. of a medicament for treatment of epithelial cell hyperplasia, fibrosis of tissue, inflammation, cancer or an immune disorder. Also a transgenic animal or cell line capable of expressing a component or an inhibitor of a **hedgehog** signaling pathway or a target pathway of the **hedgehog** signaling pathway.

REFERENCE COUNT: 8
REFERENCE(S):
(1) Deutsches Krebsforschungszentrum Stiftung Des Offentlichen Rechts; WO 9922000 A 1999 CAPLUS
(3) Fujita, E; BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS 1997, V238(2), P658 CAPLUS
(4) Johns Hopkins University School Of Medicine; WO 9952534 A 1999 CAPLUS
(5) Kabushiki Kaisha Hayashibara Seibutsu Kagaku Kenkyujo; EP 0874048 a 1998 CAPLUS
(6) Murone, M; CURRENT BIOLOGY 1999, V9(2), P76 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:190944 CAPLUS
DOCUMENT NUMBER: 132:231946
TITLE: Regulation of lung tissue by **hedgehog**-like polypeptides, and formulations and uses related thereto
INVENTOR(S): Pepicelli, Carmen; Lewis, Paula; McMahon, Andrew P.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000015246	A2	20000323	WO 1999-US20500	19990910
WO 2000015246	A3	20000720		

W: AU, CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AU 9962441	A1	20000403	AU 1999-62441	19990910
EP 1109569	A2	20010627	EP 1999-949603	19990910

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.: US 1998-99952 P 19980911
WO 1999-US20500 W 19990910

AB The present application relates to a method for modulating the growth state of a lung tissue, or a cell thereof, e.g., by ectopically contacting the tissue, in vitro or in vivo , with a **hedgehog therapeutic**, a **ptc therapeutic**, or an FGF-10 **therapeutic** in an amt. effective to alter the rate (promote or inhibit) of proliferation of cells in the lung tissue, e.g., relative to the absence of administeration of the **hedgehog therapeutic** or **ptc therapeutic**. The subject method can be used, for example, to modulate the growth state of epithelial and/or mesenchymal cells of a lung tissue, such as may be useful as part of a regimen for prevention of a disease state, or in the treatment of an existing disease state or other damage to the lung tissue.

L12 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:124058 CAPLUS
DOCUMENT NUMBER: 132:176635
TITLE: Patched genes from mammalian and invertebrate sources and their **therapeutic** uses
INVENTOR(S): Scott, Matthew P.; Goodrich, Lisa V.; Johnson, Ronald L.; Epstein, Ervin; Oro, Tony
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S., 43 pp., Cont.-in-part of U.S. 5,837,538, CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6027882	A	20000222	US 1996-656055	19960531
US 5837538	A	19981117	US 1995-540406	19951006
WO 9745541	A2	19971204	WO 1997-US9553	19970602
WO 9745541	A3	19980326		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9732274	A1	19980105	AU 1997-32274	19970602

PRIORITY APPLN. INFO.: US 1994-319745 B2 19941007
US 1995-540406 A2 19951006
US 1996-656055 A 19960531
WO 1997-US9553 W 19970602

AB Methods for isolating patched genes (**ptc** genes), homolog of the Drosophila patched gene, from mouse and human as well as from mosquito, butterfly are provided. Mutations in **ptc** gene have been identified in most exons of the gene in patients with the basal cell nevus

syndrome and in sporadic basal cell carcinomas. Using single strand conformation polymorphism anal. of DNA from 84 basal cell nevus syndrome probands and 12 sporadic basal cell carcinomas, the authors provide further evidence for the crucial role of **ptc** gene as a tumor suppressor gene. The **ptc** gene and its protein products can be used in the diagnosis of a genetic predisposition to cancer, and the identification of specific cancers having mutations in this gene, the generation of antibodies and transgenic animals as human disease models, and gene therapy.

REFERENCE COUNT: 23

REFERENCE(S): (1) Chavrier; Gene 1992, V112, P261 CAPLUS
(2) Echelard; Cell 1993, V75, P1417 CAPLUS
(4) Habuchi; Oncogene 1995, V11, P1671 CAPLUS
(5) Heemskerk; Cell 1994, V76, P449 CAPLUS
(7) Hooper; Cell 1989, V59, P751 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:764163 CAPLUS

DOCUMENT NUMBER: 131:347484

TITLE: Transgenic animals having modified **hedgehog** signal transduction for **therapeutic** applications in cancer therapy and sunscreen formulations

INVENTOR(S): Epstein, Ervin, Jr.; Scott, Matthew P.

PATENT ASSIGNEE(S): The Board of Trustees of the Leland S. Stanford, Jr. University, USA; The Regents of the University of California

SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9961582	A2	19991202	WO 1999-US11983	19990528

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-87314 19980529

AB The present invention provides transgenic animals in which the normal biol. function of one or more tumor suppressors of the patched gene family (herein "**ptc** gene") have been functionally inactivated such that, while viable at birth and into adulthood, the animal can be induced to form basal cell carcinomas at a significantly higher frequency relative to the wild-type animal, as for example, upon exposure to DNA damaging agents such as non-ionizing (e.g., UV) or ionizing radiation. Patched gene disruption was achieved by crossing over and homologous recombination and insertion recombination. As described in the pending examples, the heterozygous **ptc** knockout mice are viable at birth, but are susceptible to higher incidence of cancers when contacted with DNA damaging agents. A salient feature of these animals is that the mice can be induced to form basal cell carcinomas which, histol., are similar to BCC in humans. These transgenic animals have a heterozygous patched loss-of-function phenotype or heterozygous smoothened gain-of-function

phenotype. Homozygous animals are also generated. Hyperproliferative skin cell growth is monitored in the presence of an anti-proliferative test agent in patched +/- mice. This Hh-**Ptc** pathway may provide new diagnostic tools and new insights into tumorigenesis that can be directed toward potential therapies.

L12 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:425795 CAPLUS
DOCUMENT NUMBER: 131:69298
TITLE: Characterization of a human homolog of the Drosophila melanogaster Su(fu) gene and its involvement in **PTC**-GLI signaling
INVENTOR(S): Toftgard, Rune; Zaphiropoulos, Peter G.; Kogerman, Priit; Grimm, Thomas
PATENT ASSIGNEE(S): Karolinska Innovations AB, Swed.
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932517	A1	19990701	WO 1998-SE2383	19981218
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9919917	A1	19990712	AU 1999-19917	19981218
EP 1037920	A1	20000927	EP 1998-964640	19981218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:
SE 1997-4788 A 19971219
SE 1998-2293 A 19980626
WO 1998-SE2383 W 19981218

AB The invention provides human and mouse homologs of the Drosophila Su(fu) (suppressor of fused) gene, which is involved in the transduction of signals elicited by the interaction between the patched receptor (**PTC**) and any one of the **hedgehog** ligands (the HH-**PTC** pathway). The protein sequence for human SUFUH demonstrates 40% identity and 61% similarity to the Drosophila melanogaster sequence, and the human and mouse genes show 98% identity. Human Su(fu) was mapped to chromosome 10q24 at a region frequently lost in several tumor types, making it a candidate for a tumor suppressor gene. The human gene also maps in a region assocd. with Split hand/Split foot Malformation Type 3 (SHFM3), and based on its involvement in a signaling pathway known to regulate limb development and its demonstrated expression during mouse limb development, Su(fu) is a strong candidate for the SHFM3 gene. Addnl., given its pattern of expression during embryogenesis and strong homol. to the Drosophila homolog, the involvement of human SUFUH in **PTC**-GLI signaling was tested. Results indicated that GLI-1 and SUFUH function very closely in the signal transduction pathway and raised the possibility that they might assoc. phys. or be in the same macromol. complex, as is reported for the Drosophila counterpart. Thus, the invention provides information important for the basic understanding of a signaling pathway that is central to normal development and is often disrupted in disease. The mols. according to the present invention are useful in diagnostic and **therapeutic** methods relating to conditions assocd. with defects in said pathway, esp. certain malformations and cancer. DNA and protein sequences for the human homolog

are claimed, but they are not provided in the document.
REFERENCE COUNT: 4
REFERENCE(S): (1) Monnier, V; Current biology 1998, V8(10), P583 CAPLUS
(2) Pham, A; Genetics 1995, V140, P587 CAPLUS
(3) Preat, T; Nature 1990, V347, P87 CAPLUS
(4) Therond, P; Genetics 1996, V142, P1181 CAPLUS

L12 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:421762 CAPLUS
DOCUMENT NUMBER: 131:69289
TITLE: Human gene fused protein kinase and cDNA and **therapeutics**
INVENTOR(S): Toftgard, Rune; Zaphiropoulos, Peter G.
PATENT ASSIGNEE(S): Karolinska Innovations AB, Swed.
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932609	A1	19990701	WO 1998-SE2384	19981218
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9919918	A1	19990712	AU 1999-19918	19981218

PRIORITY APPLN. INFO.: SE 1997-4788 A 19971219
SE 1998-2292 A 19980626
WO 1998-SE2384 W 19981218

AB The present invention relates to proteins and nucleotides related to the human homolog of the Drosophila fused gene, which is involved in the transduction of signals in the **hedgehog**-patched (HH-**PTC**) pathway. The invention also relates to antibodies raised against the polypeptides according to the invention. The mols. according to the invention are useful in diagnostic and **therapeutic** methods relating to conditions assocd. with defects in said pathway.
REFERENCE COUNT: 2
REFERENCE(S): (1) Monnier, V; Current biology 1998, V8(10), P583 CAPLUS
(2) Preat, T; Letters To Nature 1990, V347, P87 CAPLUS

L12 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:282115 CAPLUS
DOCUMENT NUMBER: 130:320865
TITLE: Regulation of epithelial tissue by **hedgehog** -like polypeptides for stimulation of skin or hair formation
INVENTOR(S): Wang, Elizabeth A.
PATENT ASSIGNEE(S): Ontogeny, Inc., USA
SOURCE: PCT Int. Appl., 146 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920298	A1	19990429	WO 1998-US22227	19981020
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9911089	A1	19990510	AU 1999-11089	19981020
EP 1028741	A1	20000823	EP 1998-953814	19981020
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-955552 A 19971020
US 1998-151999 A 19980911
WO 1998-US22227 W 19981020

OTHER SOURCE(S): MARPAT 130:320865

AB The present application relates to a method for modulating the growth state of an epithelial cell by ectopically contacting the epithelial cell, in vitro or in vivo, with a **hedgehog therapeutic** or **ptc therapeutic** in an amt. effective to alter the rate (promote or inhibit) of proliferation of the epithelial cell, e.g., relative to the absence of administration of the **hedgehog therapeutic** or **ptc** (patched gene) **therapeutic**. The subject method can be used, for example, to modulate the growth state of an epithelial tissue, such as for inducing the formation of skin or other cutaneous tissue, or for inducing growth of hair.

REFERENCE COUNT: 20

REFERENCE(S):
(2) Anon; GROWTH STIMULATORS OF KERATINOCYTE AND EPIDERMAL FIBROBLASTS 1993, 10, CAPLUS
(3) Anon; HAIR GROWTH STIMULANTS CONTAINING PROTEIN KINASE-INHIBITING SULFONAMIDES 1991, 24, CAPLUS
(4) Anon; HAIR TONICS CONTAINING CYCLIC AMP DERIVATIVES 1989, 22, CAPLUS
(5) Chugai Pharmaceutical Co; JP 02273610 A 1990 CAPLUS
(6) Daiichi Seiyaku; JP 63088112 A 1988 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:172613 CAPLUS

DOCUMENT NUMBER: 130:205165

TITLE: Regulation of muscle tissue formation and/or maintenance with **hedgehog** proteins and **ptc therapeutics** and treatment or prevention of muscular disorders

INVENTOR(S): Bladgen, Chris S.; Currie, Peter D.; Ingham, Philip W.; Hughes, Simon M.

PATENT ASSIGNEE(S): Ontogeny, Inc., USA

SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9910004	A2	19990304	WO 1998-US17922	19980828
WO 9910004	A3	19990527		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,				

NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9891252	A1	19990316	AU 1998-91252	19980828
EP 1009424	A2	20000621	EP 1998-943462	19980828

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.: US 1997-57394 P 19970829
WO 1998-US17922 W 19980828

OTHER SOURCE(S): MARPAT 130:205165

AB The present application relates to a method for modulating the formation and/or maintenance of muscle tissue by ectopically contacting muscle cells, esp. muscle stem/progenitor cells, in vitro or in vivo, with a **hedgehog therapeutic** or **ptc therapeutic** in an amt. effective to alter the growth state of the treated cells. The **hedgehog therapeutic** comprises a **hedgehog** protein modified with one or more lipophilic moieties, e.g., sterols, fatty acids, or arom. hydrocarbons. The **ptc therapeutics** mimic **hedgehog**-mediated patched signal transduction by binding to patched or altering localization, protein-protein binding and/or enzymic activity of intracellular proteins involved in patched signal transduction. Such **therapeutics** included antisense oligonucleotides and protein kinase A inhibitors. Expts. in zebrafish suggested that SHH may initiate slow myoblast formation but that continued exposure is not required to trigger terminal differentiation of slow muscle fibers.

L12 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:34842 CAPLUS
DOCUMENT NUMBER: 130:105320
TITLE: Neuroprotective **hedgehog** proteins and **ptc therapeutics** (agents mimicing effects of **hedgehog** proteins on patched signalling) for treatment of stroke
INVENTOR(S): Mahanthappa, Nagesh K.
PATENT ASSIGNEE(S): Ontogeny, Inc., USA
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9900117	A2	19990107	WO 1998-US13387	19980626
WO 9900117	A3	19990401		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9881730	A1	19990119	AU 1998-81730	19980626

PRIORITY APPLN. INFO.: US 1997-883656 19970627
WO 1998-US13387 19980626

OTHER SOURCE(S): MARPAT 130:105320

AB One aspect of the present application relates to a method for limiting damage to neuronal cells from ischemic or epoxic conditions, e.g., such as may be manifest by a redn. in brain infarct vol., by administering to an individual a **hedgehog therapeutic** or **ptc**

therapeutic in an amt. effective for reducing cerebral infarct vol.

=> s "hedgehog?" and <py=1997

MISSING TERM 'AND <PY=1997'
The search profile that was entered contains a logical operator followed immediately by another operator.

=> s "hedgehog?" and "<py=1997"

L13 0 "HEDGEHOG?" AND "<PY=1997"

=> s "hedgehog?" and ">py=1997"

L14 0 "HEDGEHOG?" AND ">PY=1997"

=> s "hedgehog?" and py=1997

L15 616 "HEDGEHOG?" AND PY=1997

=> s "hedgehog?" and <py=1997

MISSING TERM 'AND <PY=1997'
The search profile that was entered contains a logical operator followed immediately by another operator.

=> s "hedgehog? and <py=1997"

L16 0 "HEDGEHOG? AND <PY=1997"

=> s "hedgehog? and >py=1997"

L17 0 "HEDGEHOG? AND >PY=1997"

=> s "hedgehog? and py<1997"

L18 0 "HEDGEHOG? AND PY<1997"

=> s "hedgehog? and py>1997"

L19 0 "HEDGEHOG? AND PY>1997"

=> s "hedgehog? and PY>1997"

L20 0 "HEDGEHOG? AND PY>1997"

=> s "hedgehog and PY>1997

MISMATCHED QUOTE '"HEDGEHOG'
Quotation marks (or apostrophes) must be used in pairs, one before and one after the expression you are setting off or masking.

=> s hedgehog and PY>1997

L21 2894 HEDGEHOG AND PY>1997

=> s hedgehog and PY<1997

2 FILES SEARCHED...
L22 3345 HEDGEHOG AND PY<1997

=> s l22 and "hedgehog polypeptide?"

```
L23          3 L22 AND "HEDGEHOG POLYPEPTIDE?"

=> dup rem

ENTER L# LIST OR (END):123

DUPLICATE IS NOT AVAILABLE IN 'CAOLD'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L23
L24           1 DUP REM L23 (2 DUPLICATES REMOVED)

=> d l24 ibib abs


L24  ANSWER 1 OF 1  BIOSIS  COPYRIGHT 2001 BIOSIS       DUPLICATE 1
ACCESSION NUMBER:   1995:457856  BIOSIS
DOCUMENT NUMBER:    PREV199598472156
TITLE:              Patterning of the neural ectoderm of Xenopus laevis by the
                    amino-terminal product of hedgehog
                    autoproteolytic cleavage.
AUTHOR(S):          Lai, Cheng-Jung; Ekker, Stephen C.; Beachy, Philip A.;
                    Moon, Randall T. (1)
CORPORATE SOURCE:   (1) Dep. Pharmacol., Univ. Washington Sch. Med., Seattle,
                    WA 98195 USA
SOURCE:             Development (Cambridge), (1995) Vol. 121, No. 8, pp.
                    2349-2360.
                    ISSN: 0950-1991.
DOCUMENT TYPE:      Article
LANGUAGE:           English
AB   The patterns of embryonic expression and the activities of Xenopus
members
     of the hedgehog gene family are suggestive of roles in neural
     induction and patterning. We report that these hedgehog
     polypeptides undergo autoproteolytic cleavage. Injection into
     embryos of mRNAs encoding Xenopus banded-hedgehog (X-bhh) or the
     amino-terminal domain (N) demonstrates that the direct inductive
     activities of X-bhh are encoded by N. In addition, both N and Xbhh
pattern
     neural tissue by elevating expression of anterior neural genes.
     Unexpectedly, an internal deletion of X-bhh (DELTA-N-C) was found to
block
     the activity of X-bhh and N in explants and to reduce dorsoanterior
     structures in embryos. As elevated hedgehog activity increases
     the expression of anterior neural genes, and as DELTA-N-C reduces
     dorsoanterior structures, these complementary data support a role for
     hedgehog in neural induction and anteroposterior patterning.


=> d his


     (FILE 'HOME' ENTERED AT 15:38:29 ON 12 AUG 2001)

     FILE 'BIOSIS, MEDLINE, CAPLUS, CAOLD' ENTERED AT 15:38:46 ON 12 AUG 2001
L1           13 S "HEDGEHOG POLYPEPTIDE?"
L2           10 DUP REM L1 (3 DUPLICATES REMOVED)
L3       276309 S POLYPEPTIDE?
L4           73 S L3 AND "HEDGEHOG?"
L5         6915 S "HEDGEHOG?"
L6           73 S L5 AND L3
L7            8 S "PTC THERAPEUTIC?"
L8            8 DUP REM L7 (0 DUPLICATES REMOVED)
L9          376 S L5 AND "PTC?"
L10           5 S L5 AND "PTC THERAPEUTIC?"
L11         177 DUP REM L9 (199 DUPLICATES REMOVED)
L12          10 S L11 AND "THERAPEUTIC?"
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L13           0 S "HEDGEHOG?" AND "<PY=1997"
L14           0 S "HEDGEHOG?" AND ">PY=1997"
L15         616 S "HEDGEHOG?" AND PY=1997
L16           0 S "HEDGEHOG? AND <PY=1997"
L17           0 S "HEDGEHOG? AND >PY=1997"
L18           0 S "HEDGEHOG? AND PY<1997"
L19           0 S "HEDGEHOG? AND PY>1997"
L20           0 S "HEDGEHOG? AND PY>1997"
L21        2894 S HEDGEHOG AND PY>1997
L22        3345 S HEDGEHOG AND PY<1997
L23           3 S L22 AND "HEDGEHOG POLYPEPTIDE?"
L24           1 DUP REM L23 (2 DUPLICATES REMOVED)

=> s ptc therapeutic and PY<1997

   2 FILES SEARCHED...
L25           0 PTC THERAPEUTIC AND PY<1997

=> s ptc and PY<1997

   2 FILES SEARCHED...
L26        3304 PTC AND PY<1997

=> s l26 and "hedgehog?"

L27          66 L26 AND "HEDGEHOG?"

=> s l27 and "hedgehog polypeptide?"

L28           0 L27 AND "HEDGEHOG POLYPEPTIDE?"

=> dup rem

ENTER L# LIST OR (END):l27

DUPLICATE IS NOT AVAILABLE IN 'CAOLD'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L27
L29           25 DUP REM L27 (41 DUPLICATES REMOVED)

=> s l29 and "ptc therapeutic?"

L30           0 L29 AND "PTC THERAPEUTIC?"

=> d l29 1-25 ibib abs


L29  ANSWER 1 OF 25  BIOSIS  COPYRIGHT 2001 BIOSIS      DUPLICATE 1
ACCESSION NUMBER:    1996:481867  BIOSIS
DOCUMENT NUMBER:     PREV199699197123
TITLE:               Regulation of patched by sonic hedgehog in the
                     developing neural tube.
AUTHOR(S):           Marigo, Valeria; Tabin, Clifford J. (1)
CORPORATE SOURCE:    (1) Dep. Genetics, Harvard Med. Sch., 200 Longwood Ave.,
                     Boston, MA 02115 USA
SOURCE:              Proceedings of the National Academy of Sciences of the
                     United States of America, (1996) Vol. 93, No. 18, pp.
                     9346-9351.
                     ISSN: 0027-8424.
DOCUMENT TYPE:       Article
LANGUAGE:            English
AB   Ventral cell fates in the central nervous system are induced by Sonic
     hedgehog, a homolog of hedgehog, a secreted Drosophila
     protein. In the central nervous system, Sonic hedgehog has been
     identified as the signal inducing floor plate, motor neurons, and
     dopaminergic neurons. Sonic hedgehog is also involved in the
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induction of ventral cell type in the developing somites. **ptc** is a key gene in the Drosophila **hedgehog** signaling pathway where it is involved in transducing the **hedgehog** signal and is also a transcriptional target of the signal. **PTC**, a vertebrate homolog of this Drosophila gene, is genetically downstream of Sonic **hedgehog** (Shh) in the limb bud. We analyze **PTC** expression during chicken neural and somite development and find it expressed in all regions of these tissues known to be responsive to Sonic **hedgehog** signal. As in the limb bud, ectopic expression of Sonic **hedgehog** leads to ectopic induction of **PTC** in the neural tube and paraxial mesoderm. This conservation of regulation allows us to use **PTC** as a marker for Sonic **hedgehog** response. The pattern of **PTC** expression suggests that Sonic **hedgehog** may play an inductive role in more dorsal regions of the neural tube than have been previously demonstrated. Examination of the pattern of **PTC** expression also suggests that **PTC** may act in a negative feedback loop to attenuate **hedgehog** signaling.

L29 ANSWER 2 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2
ACCESSION NUMBER: 1996:568389 BIOSIS
DOCUMENT NUMBER: PREV199799297745
TITLE: The role of segment polarity genes during early oogenesis in Drosophila.
AUTHOR(S): Forbes, Alexandria J.; Spradling, Allan C.; Ingham, Philip W.; Lin, Haifan (1)
CORPORATE SOURCE: (1) HHMI Res. Lab., Dep. Embryol., Carnegie Inst. Wash., 115 W. University Parkway, Baltimore, MD 21210 USA
SOURCE: Development (Cambridge), (1996) Vol. 122, No. 10, pp. 3283-3294.
ISSN: 0950-1991.
DOCUMENT TYPE: Article
LANGUAGE: English
AB In the Drosophila ovary, **hedgehog** (hh) signaling from cells near the apical tip of the germarium stimulates the proliferation and specification of somatic cells in region 2 of the germarium, 2-5 cells away from the hh-expressing cells (A. J. Forbes, H. Lin, P. Ingham and A. Spradting (1996) Development 122, 1125-1135). This report examines the role during early oogenesis of several genes that are known to function in hh-mediated signaling during embryonic and larval development (P. Ingham (1995) Current Opin. Genetics Dev. 5, 528-534). As in imaginal discs, engrailed (en) is co-expressed with hh in the germarium, while patched (**ptc**) and cubitus interruptus (ci) are expressed in somatic cells throughout the germarium and in developing egg chambers, with **ptc** expression being elevated within 10 cell diameters of the source of the hh signal. Moreover, the somatic cell overproliferation caused by ectopic hh expression is accompanied by elevated levels of **ptc** and is phenocopied in **ptc**- somatic clones. These analyses suggest that **ptc** and ci are components of the hh signaling pathway in the germarium. However, unlike embryos and imaginal discs, neither wingless (wg) nor decapentaplegic (dpp) appear to mediate the ovarian hh signal. wg is expressed in 'cap cells,' a subset of hh-expressing cells located adjacent to germ-line stem cells, but is unaffected by ectopic hh expression. Nor does the ectopic expression of wg or dpp mimic the effect of ectopic hh expression. We propose that Hh diffuses from apical cells, including cap cells, and regulates the proliferation of nearby ovarian somatic cells by antagonizing the negative effects of **ptc** on ci activity in these cells, thereby allowing the transcription of ci-dependent genes, including **ptc** itself.

L29 ANSWER 3 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3
ACCESSION NUMBER: 1996:512864 BIOSIS
DOCUMENT NUMBER: PREV199699235220
TITLE: Antagonizing cAMP-dependent protein kinase A in the dorsal

CNS activates a conserved sonic **hedgehog** signaling pathway.

AUTHOR(S): Epstein, Douglas J.; Marti, Elisa; Scott, Matthew P.; McMahon, Andrew P. (1)

CORPORATE SOURCE: (1) Dep. Mol. Cell. Biol., Harvard Univ., 16 Divinity Ave., Cambridge, MA 02138 USA

SOURCE: Development (Cambridge), (1996) Vol. 122, No. 9, pp. 2885-2894.
ISSN: 0950-1991.

DOCUMENT TYPE: Article

LANGUAGE: English

AB **Hedgehog** (Rh) signaling plays a significant role in defining the polarity of a variety of tissue types along the anterior/posterior and dorsal/ventral axes in both vertebrate and invertebrate organisms. The pathway through which Hh transduces its signal is still obscure, however, recent data have implicated the cyclic AMP-dependent protein kinase A as a negative regulator of the Hh signal transduction pathway. One of the vertebrate Hh family members, Sonic **hedgehog** (Shh), can induce ventral neural cell types both in vivo and in vitro; high concentrations induce floor plate and lower concentrations motor neurons. To investigate whether PKA plays an active role in the suppression of ventral neural differentiation, we generated transgenic embryos expressing a dominant negative form of PKA (dnPKA) in primarily dorsal aspects of the mouse CNS.

Similar to our earlier results with Shh, we observed the induction of floor plate and motor neuron markers in embryos expressing the dominant negative PKA transgene and the loss of dorsal gene expression at rostral levels. Thus suppression of PKA activity is sufficient to activate targets of the Shh signaling pathway in the vertebrate CNS suggesting that induction of ventral cell types occurs via the antagonistic action of Shh on PKA activity. Two mammalian target genes that are strongly expressed in ectopic dorsal locations in response to dnPKA are **Ptc** and Gli. As both of these are targets of Drosophila Hh signaling, our data point to an evolutionary conservation in both the mechanisms of signaling and the effectors of the signaling pathway.

L29 ANSWER 4 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 4

ACCESSION NUMBER: 1996:437871 BIOSIS

DOCUMENT NUMBER: PREV199699151477

TITLE: Transcriptional activation of **hedgehog** target genes in Drosophila is mediated directly by the Cubitus interruptus protein, a member of the GLI family of zinc finger DNA-binding proteins.

AUTHOR(S): Alexandre, Cyrille; Jacinto, Antonio; Ingham, Philip W. (1)

CORPORATE SOURCE: (1) Mol. Embryol. Lab., Imperial Cancer Res. Fund, London WC2A 3PX UK

SOURCE: Genes & Development, (1996) Vol. 10, No. 16, pp. 2003-2013.
ISSN: 0890-9369.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Members of the **Hedgehog** (Hh) family of secreted proteins have been identified recently as key signaling molecules that regulate a variety of inductive interactions central to the development of both Drosophila and vertebrates. Despite their widespread importance, the way in which Hh signals are transduced inside the cell remains poorly understood. The best candidate for a transcription factor that mediates Hh signaling in Drosophila is the product of the cubitus interruptus (ci) gene, a zinc finger protein that exhibits significant homology to protein

products of the vertebrate GLI gene family. Here, we show that elevated levels of Ci are sufficient to activate patched (**ptc**) and other hh target genes, even in the absence of kh activity. We also show that Ci can function as a transcriptional activator in yeast and demonstrate that the zinc finger domain of the protein is sufficient for its target specificity. Finally, we identify sequences in the promoter region of the **ptc** gene, a primary target of Hh signaling, that are identical to the consensus-binding sequence of the GLI protein and are required for reporter gene expression in response to Hh activity. Taken together, our results strongly support the role for Ci as the transcriptional activator that mediates hh signaling.

L29 ANSWER 5 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 5
ACCESSION NUMBER: 1996:332577 BIOSIS
DOCUMENT NUMBER: PREV199699054933
TITLE: Human homolog of patched, a candidate gene for the basal cell nevus syndrome.
AUTHOR(S): Johnson, Ronald L.; Rothman, Alana L.; Xie, Jingwu; Goodrich, Lisa V.; Bare, John W.; Bonifas, Jeannette M.; Quinn, Anthony G.; Myers, Richard M.; Cox, David R.; Epstein., Ervin H., Jr.; Scott, Matthew P. (1)
CORPORATE SOURCE: (1) Dep. Dev. Biology, Howard Hughes Med. Inst., Stanford Univ. Sch. Med., Stanford, CA 94305-5427 USA
SOURCE: Science (Washington D C), (1996) Vol. 272, No. 5268, pp. 1668-1671.
ISSN: 0036-8075.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The basal cell nevus syndrome (BCNS) is characterized by developmental abnormalities and by the postnatal occurrence of cancers, especially basal cell carcinomas (BCCs), the most common human cancer. Heritable mutations in BCNS patients and a somatic mutation in a sporadic BCC were identified in a human homolog of the Drosophila patched (**ptc**) gene. The **ptc** gene encodes a transmembrane protein that in Drosophila acts in opposition to the **Hedgehog** signaling protein, controlling cell fates, patterning, and growth in numerous tissues. The human **PTC** gene appears to be crucial for proper embryonic development and for tumor suppression.

L29 ANSWER 6 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 6
ACCESSION NUMBER: 1996:409153 BIOSIS
DOCUMENT NUMBER: PREV199699131509
TITLE: Regulation of rate of cartilage differentiation by Indian **hedgehog** and PTH-related protein.
AUTHOR(S): Vortkamp, Andrea; Lee, Kaechoong; Lanske, Beate; Segre, Gino V.; Kronenberg, Henry M.; Tabin, Clifford J. (1)
CORPORATE SOURCE: (1) Dep. Genetics, Harvard Med. Sch., Boston, MA 02115 USA
SOURCE: Science (Washington D C), (1996) Vol. 273, No. 5275, pp. 613-622.
ISSN: 0036-8075.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Proper regulation of chondrocyte differentiation is necessary for the morphogenesis of skeletal elements, yet little is known about the molecular regulation of this process. A chicken homolog of Indian **hedgehog** (Ihh), a member of the conserved **Hedgehog** family of secreted proteins that is expressed during bone formation, has now been isolated. Ihh has biological properties similar to those of Sonic **hedgehog** (Shh), including the ability to regulate the conserved targets Patched (**Ptc**) and Gli. Ihh is expressed in the prehypertrophic chondrocytes of cartilage elements, where it regulates the rate of hypertrophic differentiation. Misexpression of Ihh prevents proliferating chondrocytes from initiating the hypertrophic

differentiation process. The direct target of Ihh signaling is the perichondrium, where Gli and **Ptc** flank the expression domain of Ihh. Ihh induces the expression of a second signal, parathyroid hormone-related protein (PTHrP), in the periarticular perichondrium. Analysis of PTHrP (-/-) mutant mice indicated that the PTHrP protein signals to its receptor in the prehypertrophic chondrocytes, thereby blocking hypertrophic differentiation. In vitro application of **Hedgehog** or PTHrP protein to normal or PTHrP (-/-) limb explants demonstrated that PTHrP mediates the effects of Ihh through the formation of a negative feedback loop that modulates the rate of chondrocyte differentiation.

L29 ANSWER 7 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 7
ACCESSION NUMBER: 1996:535148 BIOSIS
DOCUMENT NUMBER: PREV199699257504
TITLE: Dual roles for Patched in sequestering and transducing **Hedgehog**.
AUTHOR(S): Chen, Yu; Struhl, Gary
CORPORATE SOURCE: Howard Hughes Med. Inst., Dep. Genetics and Development, Columbia Univ. Coll. Physicians and Surgeons, New York, NY 10032 USA
SOURCE: Cell, (1996) Vol. 87, No. 3, pp. 553-563. ISSN: 0092-8674.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Secreted proteins of the **Hedgehog** (Hh) family have diverse organizing roles in animal development. Recently, a serpentine protein Smoothened (Smo) has been proposed as a Hh receptor. Here, we present evidence that implicates another multiple-pass transmembrane protein, Patched (**Ptc**), in Hh reception and suggests a novel signal transduction mechanism in which Hh binds to **Ptc**, or a **Ptc**-Smo complex, and thereby induces Smo activity. Our results also show that **Ptc** limits the range of Hh action; we provide evidence that high levels of **Ptc** induced by Hh serve to sequester any free Hh and therefore create a barrier to its further movement.

L29 ANSWER 8 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 8
ACCESSION NUMBER: 1996:122958 BIOSIS
DOCUMENT NUMBER: PREV199698695093
TITLE: Conservation of the **hedgehog**/patched signaling pathway from flies to mice: Induction of a mouse patched gene by **hedgehog**.
AUTHOR(S): Goodrich, Lisa V.; Johnson, Ronald L.; Milenkovic, Ljiljana; McMahon, Jill A.; Scott, Matthew P. (1)
CORPORATE SOURCE: (1) Dep. Dev. Biol., Howard Hughes Med. Inst., Stanford Univ. Sch. Med., Stanford, CA 94305-5427 USA
SOURCE: Genes & Development, (1996) Vol. 10, No. 3, pp. 301-312. ISSN: 0890-9369.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The signaling protein **Hedgehog** (Hh) controls cell fate and polarizes tissues in both flies and vertebrates. In flies, Hh exerts its effects by opposing the function of a novel transmembrane protein, Patched, while also locally inducing patched (**ptc**) transcription. We have identified a mouse homolog of **ptc** which in many tissues is transcribed near cells making either Sonic or Indian **hedgehog**. In addition, ectopic Sonic **hedgehog** expression in the mouse central nervous system induces **ptc** transcription. As in flies, mouse **ptc** transcription appears to be indicative of **Hedgehog** signal reception. The results support the existence of a conserved signaling pathway used for pattern formation in insects and mammals.

L29 ANSWER 9 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 9
ACCESSION NUMBER: 1997:20622 BIOSIS

DOCUMENT NUMBER: PREV199799319825
TITLE: Biochemical evidence that patched is the **hedgehog** receptor.
AUTHOR(S): Marigo, Valeria; Davey, Robert A.; Zuo, Yi; Cunningham, James M.; Tabin, Clifford J. (1)
CORPORATE SOURCE: (1) Dep. Genetics, Harvard Med. Sch., 200 Longwood Ave., Boston, MA 02115 USA
SOURCE: Nature (London), (1996) Vol. 384, No. 6605, pp. 176-179. ISSN: 0028-0836.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The protein Sonic **hedgehog** (Shh) is essential for a variety of patterning events during development. It is the signal from the notochord that induces ventral cell fate in the neural tube and somites and is the polarizing signal for patterning of the anterior-posterior axis of the developing limb bud. Because of these and other inductive functions of Shh, it is important to understand how the **Hedgehog** (Hh) signal is received by the target cells. Here we describe binding studies using labelled Shh that strongly suggest that the Hh receptor is encoded by patched (**ptc**), a gene first identified in genetic screens in Drosophila.

L29 ANSWER 10 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 10
ACCESSION NUMBER: 1996:282910 BIOSIS
DOCUMENT NUMBER: PREV199699005266
TITLE: The fu gene discriminates between pathways to control dpp expression in Drosophila imaginal discs.
AUTHOR(S): Sanchez-Herrero, Ernesto; Couso, Juan Pablo; Capdevila, Javier; Guerrero, Isabel (1)
CORPORATE SOURCE: (1) Centro Biologia Molecular, 'Severo Ochoa', Univ. Autonoma Madrid, Cantoblanco, 28049 Madrid Spain
SOURCE: Mechanisms of Development, (1996) Vol. 55, No. 2, pp. 159-170.
ISSN: 0925-4773.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The genes decapentaplegic (dpp) and wingless (wg), which encode secreted factors of the TGF-beta and Wnt families, respectively, are required for the proper development of the imaginal discs. The expression of these genes must be finely regulated since their ectopic expression induces overgrowth and pattern alterations in wings and legs. Genes like patched (**ptc**) and costal-2 (cos-2), and the gene encoding the catalytic subunit of the protein kinase A gene (pkA) are required to restrict dpp and wg expression in their proper positions. We show here that some mutations in the cubitus interruptus (ci) gene also show ectopic dpp expression in the wing disc. We have also analyzed the functional hierarchy between these genes and the gene fused (fu), in the activation of dpp by the **hedgehog** (hh) signal. fu is required to transmit the hh signal in imaginal discs, since fu mutations rescue the phenotype due to the ectopic hh expression or to the lack of **ptc** activity. fu is also required for the activation of engrailed (en) caused when hh is ectopically activated in the wing disc. By contrast, fu mutations do not rescue the phenotypic consequences of the abnormal ci, cos-2 or pkA activity. Although fu, cos-2 and ci probably form part of the same pathway that controls dpp expression, pkA probably controls dpp transcription by a different pathway.

L29 ANSWER 11 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 11
ACCESSION NUMBER: 1997:18893 BIOSIS
DOCUMENT NUMBER: PREV199799318096
TITLE: The tumour-suppressor gene patched encodes a candidate receptor for Sonic **hedgehog**.

AUTHOR(S): Stone, Donna M.; Hynes, Mary; Armanini, Mark; Swanson, Todd
A.; Gu, Qimin; Johnson, Ronald L.; Scott, Matthew P.; Pennica, Diane; Goddard, Audrey; Phillips, Heidi; Noll, Markus; Hooper, Joan E.; De Sauvage, Frederic; Rosenthal, Arnon (1)
CORPORATE SOURCE: (1) Dep. Neurosci., Genentech Inc., 460 Point San Bruno Boulevard, South San Francisco, CA 94080 USA
SOURCE: Nature (London), (1996) Vol. 384, No. 6605, pp. 129-134. ISSN: 0028-0836.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The protein Sonic **hedgehog** (Shh) controls patterning and growth during vertebrate development. Here we demonstrate that it binds Patched (vPtc), which has been identified as a tumour-suppressor protein in basal cell carcinoma, with high affinity. We show that **Ptc** can form a physical complex with a newly cloned vertebrate homologue of the Drosophila protein Smoothened (vSmo), and that vSmo is coexpressed with vPtc in many tissues but does not bind Shh directly. These findings, combined with available genetic evidence from Drosophila, support the hypothesis that **Ptc** is a receptor for Shh, and that vSmo could be a signalling component that is linked to **Ptc**.

L29 ANSWER 12 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 12
ACCESSION NUMBER: 1995:126214 BIOSIS
DOCUMENT NUMBER: PREV199598140514
TITLE: Drawing a stripe in Drosophila imaginal disks: Negative regulation of decapentaplegic and patched expression by engrailed.
AUTHOR(S): Sanicola, Michele; Sekelsky, Jeff; Elson, Sarah; Gelbart, William M. (1)
CORPORATE SOURCE: (1) Harvard Univ., 16 Divinity Ave., Cambridge, MA 02138 USA
SOURCE: Genetics, (1995) Vol. 139, No. 2, pp. 745-756. ISSN: 0016-6731.
DOCUMENT TYPE: Article
LANGUAGE: English
AB During development of the Drosophila adult appendage precursors. the larval imaginal disks, the decapentaplegic (dpp) gene is expressed in a stripe just anterior to the anterior/posterior (A/P) compartment boundary.
Here, we investigate the genetic controls that lead to production of this stripe. We extend previous observations on leaky engrailed (en) mutations by showing that mutant clones completely lacking both en and invected (inv) activity ectopically express dpp-lacZ reporter genes in the posterior compartment, where dpp activity ordinarily is repressed. Similarly, patched (**ptc**) is also ectopically expressed in such posterior compartment en-inv- null clones. In contrast, these en-inv- clones exhibit loss of **hedgehog** (hh) expression. We suggest that the absence of dpp expression in the posterior compartment is due to direct repression by en. Ubiquitious expression of en in imaginal disks, produced by a hs-en construct, eliminates the expression of dpp-lacZ in its normal A/P boundary stripe. We identify three in vitro Engrailed binding sites in one of our dpp-lacZ reporter gene. Mutagenesis of these Engrailed binding sites results in ectopic expression of this reporter gene, but does not alter the normal stripe of expression at the A/P boundary. We propose that the en-hh-**ptc** regulatory loop that is responsible for segmental expression of wingless in the embryo is reutilized in imaginal disks to create a stripe of dpp expression along the A/P compartment boundary.

L29 ANSWER 13 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 13
ACCESSION NUMBER: 1995:173102 BIOSIS
DOCUMENT NUMBER: PREV199598187402
TITLE: Signal transduction by cAMP-dependent protein kinase A in Drosophila limb patterning.

AUTHOR(S): Lepage, Thierry; Cohen, Stephen M. (1); Diaz-Benjumea, Fernando J.; Parkhurst, Susan M.
CORPORATE SOURCE: (1) Div. Basic Sci., A1-162 Fred Hutchinson Cancer Res. Cent., Seattle, WA 98104 USA
SOURCE: Nature (London), (1995) Vol. 373, No. 6516, pp. 711-715. ISSN: 0028-0836.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Interaction between distinctly specified cells in adjacent compartments establishes organizing centres that control growth and specify cell fate in the developing limbs of Drosophila. Localized expression of the secreted **Hedgehog** protein (Hh) by cells in the posterior compartment" induces expression of the secreted signalling molecules decapentaplegic (dpp) or wingless (wg) in nearby anterior cells. wg and dpp in turn organize spatial pattern in the wing and leg imaginal discs. The Hh signal is thought to act by antagonizing the ability of the patched (**ptc**) gene product to repress wg and dpp expression. Here we present evidence that removing activity of the gene encoding cyclic AMP-dependent protein kinase A (pka) is functionally equivalent to removing **ptc** activity or to providing cells with the Hh signal. These findings suggest that cyclic AMP-dependent protein kinase A is a component of the signal transduction pathway through which Hh and **Ptc** direct localized expression of dpp (or wg) and establish the compartment boundary organizer.

L29 ANSWER 14 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 14
ACCESSION NUMBER: 1995:173214 BIOSIS
DOCUMENT NUMBER: PREV199598187514
TITLE: Function of protein kinase A in **hedgehog** signal transduction and Drosophila imaginal disc development.
AUTHOR(S): Li, Willis (1); Ohlmeyer, Johanna Talavera (1); Lane, Mary Ellen; Kalderon, Daniel (1)
CORPORATE SOURCE: (1) Dep. Biol. Sci., Columbia Univ., New York, NY 10027 USA
SOURCE: Cell, (1995) Vol. 80, No. 4, pp. 553-562. ISSN: 0092-8674.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Reduced protein kinase A (PKA) activity in anterior imaginal disc cells leads to cell-autonomous induction of decapentaplegic (dpp), wingless (wg), and patched (**ptc**) transcription that is independent of **hedgehog** (hh) gene activity. The resulting nonautonomous adult wing and leg pattern duplications are largely due to induced dpp and wg expression and resemble phenotypes elicited by ectopic hh expression. Inhibition of PKA in anterior cells close to the posterior compartment can substitute for hh activity to promote growth of imaginal discs, whereas overexpression of PKA can counteract transcriptional induction of **ptc** by hh in these cells. PKA therefore appears to be an integral component of the mechanism by which hh regulates the expression of key patterning molecules in imaginal discs.

L29 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:409133 CAPLUS
DOCUMENT NUMBER: 122:183472
TITLE: **Hedgehog** and beyond
AUTHOR(S): Perrimon, Norbert
CORPORATE SOURCE: Department of Genetics, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Cell (Cambridge, Mass.) (**1995**), 80(4), 517-20
CODEN: CELLB5; ISSN: 0092-8674
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 24 refs., on: **hedgehog** (Hh) initiation of both

short-range and long-range signalling; feedback loops; 2 distinct Hh signalling pathways; role of protein kinase A in Hh signalling; and the role of protein **Ptc** in regulation of protein kinase A activity.

L29 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:345631 CAPLUS
DOCUMENT NUMBER: 122:179411
TITLE: Invisible deep grooves between en/hh expressing cells and wg expressing cells
AUTHOR(S): Nakano, Yoshiro
CORPORATE SOURCE: Mitsubishi Kasei Inst. Life Sci., Machida, 194, Japan
SOURCE: Jikken Igaku (**1995**), 13(3), 319-24
CODEN: JIIGEF; ISSN: 0288-5514
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review, with 29 refs., on the formation of segment and parasegment in Drosophila in relation to the expression of hh/en and wg, different expression timing of segment polarity genes, and resp. expression regulation by the interaction of the products of segment polarity genes such as wg gene with Hh protein. Participation in wg expression and its regulation by Hh, **Ptc**, CiD and Fused, and interaction between en/hh expressing cells and wg expressing cells are discussed.

L29 ANSWER 17 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 15
ACCESSION NUMBER: 1994:270548 BIOSIS
DOCUMENT NUMBER: PREV199497283548
TITLE: Localized expression of sloppy paired protein maintains the polarity of Drosophila parasegments.
AUTHOR(S): Cadigan, Kenneth M. (1); Grossniklaus, Ueli; Gehring, Walter J.
CORPORATE SOURCE: (1) Howard Hughes Med. Inst., Dep. Developmental Biol., Beckman Center, Stanford Univ. Sch. Med., Stanford, CA 94305-5428 USA
SOURCE: Genes & Development, (1994) Vol. 8, No. 8, pp. 899-913. ISSN: 0890-9369.
DOCUMENT TYPE: Article
LANGUAGE: English
AB During germ-band extension in the Drosophila embryo, intercellular communication is required to maintain gene expression patterns initiated at cellular blastoderm. For example, the wingless (wg) single-cell-wide stripe in each parasegment (PS) is dependent on a signal from the adjacent, posterior cells, which express engrailed (en). This signal is thought to be the **hedgehog** (hh) gene product, which antagonizes the activity of patched (**ptc**), a repressor of wg expression. Genetic evidence indicates that the hh signal is bidirectional, but wg transcription is only derepressed on the anterior side of the en/hh stripes. To explain the asymmetric response of the wg promoter to the hh signal, current models predict that each PS is divided into cells that are competent to express either wg or en, but not both. The sloppy paired (slp) locus contains two transcription units, both encoding proteins containing a forkhead domain, a DNA-binding motif. Removal of slp gene function causes embryos to exhibit a severe pair-rule/segment polarity phenotype. We show that the en stripes expand anteriorly in slp mutant embryos and that slp activity is an absolute requirement for maintenance of wg expression at the same time that wg transcription is dependent on hh. The slp proteins are expressed in broad stripes just anterior of the en-positive cells, overlapping the narrow wg stripes. We propose that by virtue of their ability to activate wg and repress en expression, the distribution of the slp proteins define the wg-competent and en-competent groups. Consistent with this hypothesis, ubiquitous expression of slp protein throughout the PS abolishes en expression and, in **ptc** mutant embryos, results in a near ubiquitous distribution of wg transcripts. In addition to demonstrating the role of slp in maintaining segment polarity, our results suggest that slp works in, or parallel with,

the **ptc**/hh signal transduction pathway to regulate wg transcription.

L29 ANSWER 18 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 16
ACCESSION NUMBER: 1995:77574 BIOSIS
DOCUMENT NUMBER: PREV199598091874
TITLE: Distinct pathways for autocrine and paracrine Wingless signalling in Drosophila embryos.
AUTHOR(S): Hooper, Joan E.
CORPORATE SOURCE: Dep. Cell. Structural Biol., Univ. Colorado Health Sci. Cent., Denver, CO 80262 USA
SOURCE: Nature (London), (1994) Vol. 372, No. 6505, pp. 461-464. ISSN: 0028-0836.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Two secreted proteins, Wingless-1,2 and **Hedgehog**-3,4, instruct cell fates within the segmented epidermis of Drosophila embryos (reviewed in ref. 5). Wingless (Wg) is expressed by the most posterior cells in each parasegment; **Hedgehog** (Hh) is expressed in the most anterior cells of the next parasegment. Immediately after gastrulation, the two cell types are mutually dependent-6,7. Local Wg signalling stabilizes Hh expression-8-10 and local Hh signalling stabilizes Wg expression-11,12. Direct Wg autoregulation (autocrine signalling) is masked by its paracrine role in maintaining hh, which in turn maintains wg. I have used zeste-white3 (zw3)-13 and patched (**ptc**)-11,14 mutant backgrounds to uncouple genetically this positive-feedback loop and to study autocrine Wg signalling. I report here that direct Wg autoregulation differs from Wg signalling to adjacent cells in the importance of fused (fu), smoothened (smo) and cubitus interruptus (ci) relative to zw3 and armadillo (arm). I also find that Wg autoregulation during this early hh-dependent phase differs from later Wg autoregulation-15 by lack of gooseberry (gsb) participation.

L29 ANSWER 19 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 17
ACCESSION NUMBER: 1994:391785 BIOSIS
DOCUMENT NUMBER: PREV199497404785
TITLE: Patched overexpression causes loss of wingless expression in Drosophila embryos.
AUTHOR(S): Schuske, Kim; Hooper, Joan E.; Scott, Matthew P. (1)
CORPORATE SOURCE: (1) Dep. Developmental Biol. Gentics Howard Hughes Med. Inst., Stanford Univ. Sch. Med., Stanford, CA 94305-5427 USA
SOURCE: Developmental Biology, (1994) Vol. 164, No. 1, pp. 300-311.
ISSN: 0012-1606.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The patched (**ptc**) segment polarity gene of Drosophila encodes a transmembrane protein involved in cell signaling that establishes pattern within the segment. In the posterior half of the parasegment Patched protein represses transcription of the wingless (wg) gene by an unknown mechanism. In the most posterior row of cells in each parasegment this repression is neutralized by a signal possibly carried by the product of the **hedgehog** gene, allowing wg expression. High levels of Patched expression might therefore overcome the repression and repress wg in all cells. Here we use a heat shock-inducible promoter to transiently express high levels of Patched in all cells. A single pulse of Patched transgene expression has little or no effect on the segmental pattern, as has been previously reported. Repeated pulses of Patched production drastically alter the segment pattern to mimic embryos lacking one of the wg class of segment polarity genes. We observe repression of wg and gooseberry (a wg class gene) transcription in the germband ectoderm but

not in the head. Expression of two other segment polarity genes, engrailed
and cubitus interruptus, is unaffected. Thus excess Patched is capable of overcoming the neutralizing signal.

L29 ANSWER 20 OF 25 MEDLINE
ACCESSION NUMBER: 94116449 MEDLINE
DOCUMENT NUMBER: 94116449 PubMed ID: 8287799
TITLE: Segment polarity gene interactions modulate epidermal patterning in Drosophila embryos.
AUTHOR: Bejsovec A; Wieschaus E
CORPORATE SOURCE: Department of Molecular Biology, Princeton University, New Jersey 08544.
CONTRACT NUMBER: HD 15587 (NICHD)
SOURCE: DEVELOPMENT, **(1993 Oct)** 119 (2) 501-17.
Journal code: ECW; 8701744. ISSN: 0950-1991.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199402
ENTRY DATE: Entered STN: 19940312
Last Updated on STN: 19940312
Entered Medline: 19940222

AB Each segment of a Drosophila larva shows a precisely organized pattern of cuticular structures, indicating diverse cellular identities in the underlying epidermis. Mutations in the segment polarity genes alter the cuticle pattern secreted by the epidermal cells; these mutant patterns provide clues about the role that each gene product plays in the development of wild-type epidermal pattern. We have analyzed embryos that are multiply mutant for five key patterning genes: wingless, patched, engrailed, naked and **hedgehog**. Our results indicate that wild-type activity of these five segment polarity genes can account for most of the ventral pattern elements and that their gene products interact
extensively to specify the diverse cellular identities within the epidermis. Two pattern elements can be correlated with individual gene action: wingless is required for formation of naked cuticle and engrailed is required for formation of the first row of denticles in each abdominal denticle belt. The remaining cell types can be produced by different combinations of the five gene activities. wingless activity generates the diversity of cell types within the segment, but each specific cell identity depends on the activity of patched, engrailed, naked and **hedgehog**. These molecules modulate the distribution and interpretation of wingless signalling activity in the ventral epidermal cells and, in addition, each can contribute to pattern through a pathway independent of the wingless signalling pathway.

L29 ANSWER 21 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 18
ACCESSION NUMBER: 1993:229476 BIOSIS
DOCUMENT NUMBER: PREV199395120651
TITLE: Regulation of wingless transcription in the Drosophila embryo.
AUTHOR(S): Ingham, P. W. (1); Hidalgo, A.
CORPORATE SOURCE: (1) ICRF Dev. Biol. Unit, Dep. Zool., South Parks Rd., Oxford OX1 3PS UK
SOURCE: Development (Cambridge), (1993) Vol. 117, No. 1, pp. 283-291.
ISSN: 0950-1991.
DOCUMENT TYPE: Article
LANGUAGE: English

AB The segment polarity gene wingless (wg) is expressed in a complex pattern during embryogenesis suggesting that it plays multiple roles in the development of the embryo. The best characterized of these is its role in cell pattening in each parasegment, a process that requires the activity of other segment polarity genes including patched (**ptc**) and

hedgehog (hh). Here we present further evidence that **ptc** and hh encode components of a signal transduction pathway that regulate the expression of wg transcription following its activation by pair-rule genes. We also show that most other aspects of wg expression are independent of this regulatory network.

L29 ANSWER 22 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 19
ACCESSION NUMBER: 1994:346908 BIOSIS
DOCUMENT NUMBER: PREV199497359908
TITLE: Genetic analysis of **hedgehog** signalling in the Drosophila embryo.
AUTHOR(S): Forbes, A. J.; Nakano, Y.; Taylor, A. M.; Ingham, P. W. (1)
CORPORATE SOURCE: (1) Mol. Embryol. Lab., ICRF Dev. Biol. Unit, Dep. Zool., South Parks Rd., Oxford OX 1 3PS UK
SOURCE: Development (Cambridge), (1993) Vol. 0, No. SUPPL., pp. 115-124.
ISSN: 0950-1991.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The segment polarity genes play a fundamental role in the patterning of cells within individual body segments of the Drosophila embryo. Two of these genes wingless (wg) and **hedgehog** (hh) encode proteins that enter the secretory pathway and both are thought to act by instructing the fates of cells neighbouring those in which they are expressed. Genetic analysis has identified the transcriptional activation of wg as one of the targets of hh activity: here we present evidence that transduction of the hh-encoded signal is mediated by the activity of four other segment polarity genes, patched, fused, costal-2 and cubitus interruptus. The results of our genetic epistasis analysis together with the molecular structures of the products of these genes where known, suggest a pathway of interactions leading from reception of the hhencoded signal at the cell membrane to transcriptional activation in the cell nucleus. We have also found that transcription of patched is regulated by the same pathway and describe the identification of cis-acting upstream elements of the **ptc** transcription unit that mediate this regulation.

L29 ANSWER 23 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 20
ACCESSION NUMBER: 1993:385733 BIOSIS
DOCUMENT NUMBER: PREV199396061033
TITLE: Contrasting distributions of patched and **hedgehog** proteins in the Drosophila embryo.
AUTHOR(S): Taylor, A. M.; Nakano, Y.; Mohler, J.; Ingham, P. W. (1)
CORPORATE SOURCE: (1) ICRF Biol. Unit, Dep. Zool., South Parks Road, Oxford OX1 3PS UK
SOURCE: Mechanisms of Development, (1993) Vol. 42, No. 1-2, pp. 89-96.
ISSN: 0925-4773.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The segment polarity genes patched (**ptc**) and **hedgehog** (hh) are thought to encode a receptor and signal molecule respectively, components of a signal transduction pathway that regulates the transcription of the wingless gene in the Drosophila embryo. Here we describe the production of antibodies specific for the products of these two genes and the patterns of protein distribution that they reveal in the developing embryo. The results are consistent with the hh protein being secreted by cells in which it is expressed and support a role for **ptc** in the reception of the putative hh encoded signal.

L29 ANSWER 24 OF 25 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 21
ACCESSION NUMBER: 1993:140738 BIOSIS